

Art Unit: 1624

1. This application is in condition for allowance except for the presence of the non-elected subject matter in the definitions of “A” and “R¹” (without traverse). Accordingly, the non-elected subject matter has been deleted. Also, the provisos drawn to furan, pyrrole, oxazole, thiazole or imidazole are no longer applicable, and thus, are deleted as well.

EXAMINER’S AMENDMENT

2. An examiner’s amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Claim 1 (also, see attachment):

Line 4, in the definition of A, delete “, **furan, pyrrole, imidazole, thiazole or oxazole**”;

Line 5, in the definition of R¹, delete “**or a 5- to 7-membered heteroaromatic ring containing one to three heteroatoms selected independently from oxygen, nitrogen or sulfur**”;

Line 6, after the phrase ‘said phenyl’, delete “**or heteroaromatic ring**”;

Line 29, the first proviso, after the word ‘thiophene,’ delete “**furan or pyrrole**”;

Line 30, delete “**and**”

Lines 31-32, delete the entire second proviso, that is, delete “**when A represents oxazole, thiazole or imidazole, then R¹ is not 3-pyridyl or 5-pyrimidyl.**”

Art Unit: 1624

Claim 3 (also, see attachment):

Line 2, insert the word – and – after ‘CR²,’ and delete “O and NR²⁵,”

Cancel claims 4 and 5;

Claim 8 (also see attachment): delete the 6th compound, 8th compound, 44th - 47th compounds, 53rd, 55th, 57th compounds, 60th – 64th compounds, 68th – 77th compounds, 84th – 87th compounds.

Applicant : Andrew Baxter et al.
 Serial No. : 09/868,884
 Filed : June 22, 2001
 Page : 2 of 14

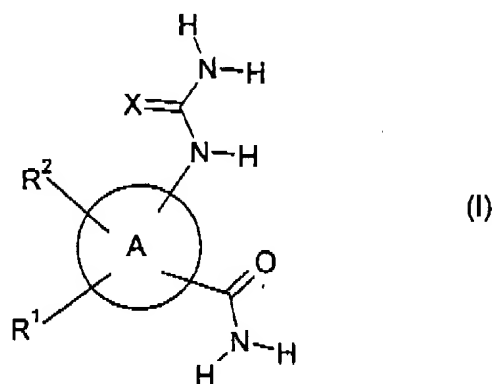
Attorney's Docket No.: 06275-233001 / Z70663-1P US

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Previously presented) A compound of formula (I)



in which:

A represents thiophene, ~~furán, pyrrole, imidazole, thiazole or oxazole,~~

R¹ represents a phenyl group or a 5- to 7-membered heteroaromatic ring containing one ~~to three heteroatoms selected independently from oxygen, nitrogen or sulfur, said phenyl or heteroaromatic ring~~ being optionally substituted by one or more substituents selected independently from halogen, cyano, nitro, -NR³R⁴, -CONR⁵R⁶, -COOR⁷, -NR⁸COR⁹, -SR¹⁰, -S(O)_mR¹⁰, -S(O)₂NR⁵R⁶, -NR⁸SO₂R¹⁰, C₁-C₆ alkyl, trifluoromethyl, -(CH₂)_nR¹¹, -O(CH₂)_nR¹¹ or -OR¹²;

Applicant : Andrew Baxter et al.
Serial No. : 09/868,884
Filed : June 22, 2001
Page : 3 of 14

Attorney's Docket No.: 06275-233001 / Z70663-1P US

R^2 represents hydrogen, halogen, cyano, nitro, $-NR^{13}R^{14}$, $-CONR^{15}R^{16}$, $-COOR^{17}$, $-NR^{18}COR^{19}$, $-S(O)_mR^{20}$, $-S(O)_2NR^{15}R^{16}$, $-NR^{18}SO_2R^{20}$, C_1 - C_2 alkyl, trifluoromethyl, C_2 - C_3 alkenyl, C_2 - C_3 alkynyl, trifluoromethoxy, C_1 - C_2 alkoxy or C_1 - C_2 alkanoyl;

X represents oxygen or sulfur;

each of R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} and R^{12} independently represent a hydrogen atom or C_1 - C_6 alkyl;

R^{11} represents $NR^{21}R^{22}$ where R^{21} and R^{22} are independently hydrogen or C_1 - C_6 alkyl optionally substituted by C_1 - C_4 alkoxy; or R^{21} and R^{22} together with the nitrogen atom to which they are attached form a 5- or 6-membered saturated ring optionally containing a further O, S or NR^{23} group where R^{23} is hydrogen or C_1 - C_6 alkyl; or R^{11} represents OR^{24} where R^{24} represents C_1 - C_6 alkyl;

each of R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} , R^{19} and R^{20} independently represent a hydrogen atom or C_1 - C_2 alkyl;

m represents an integer 0, 1 or 2;

n represents an integer 2, 3 or 4;

and optical isomers, racemates, and tautomers thereof and pharmaceutically acceptable salts or solvates thereof;

provided that:

when A represents thiophene, ~~fur~~an or pyrrole, then R^1 is not 4-pyridinyl or 3-pyrazolyl;

and

when A represents oxazole, thiazole or imidazole, then R^1 is not 3-pyridinyl or 5-

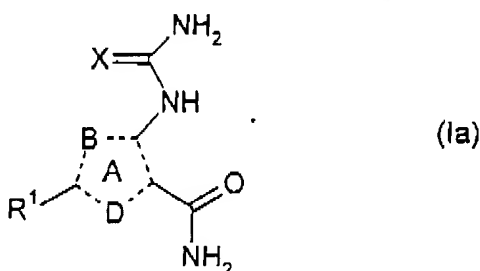
~~pyrimidyl.~~

2. (Original) A compound of formula (I), according to claim 1, wherein X represents oxygen.

Applicant : Andrew Baxter et al.
Serial No. : 09/868,884
Filed : June 22, 2001
Page : 4 of 14

Attorney's Docket No.: 06275-233001 / Z70663-1P US

3. (Previously presented) A compound of formula (I), according to Claim 1, in which the group A is substituted as shown below in formula (Ia), where B and D are selected from CR², and S, O and NR²⁵, where R² is as defined in Claim 1 and R²⁵ is hydrogen or C₁-C₆ alkyl:



4. ~~(Previously presented) A compound according to claim 1 in which the ring A is thiophene.~~

5. ~~(Previously presented) A compound according to claim 1 in which R¹ represents optionally substituted phenyl.~~

6. (Previously presented) A compound according to claim 1 in which R² represents H or methyl.

7. (Original) A compound according to claim 6 in which R² represents H.

8. (Original) A compound of formula (I), according to claim 1, selected from:

3-[(aminocarbonyl)amino]-5-phenyl-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-(3-chlorophenyl)-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-(4-fluorophenyl)-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-(4-chlorophenyl)-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-(4-isobutylphenyl)-2-thiophenecarboxamide;

~~3-[(aminocarbonyl)amino]-5-(2-thienyl)-2-thiophenecarboxamide;~~

3-[(aminocarbonyl)amino]-5-(4-methoxyphenyl)-2-thiophenecarboxamide;

Applicant : Andrew Baxter et al.
Serial No. : 09/868,884
Filed : June 22, 2001
Page : 5 of 14

Attorney's Docket No.: 06275-233001 / Z70663-1P US

~~3-[(aminocarbonyl)amino]-5-(3-thienyl)-2-thiophenecarboxamide;~~

3-[(aminocarbonyl)amino]-5-(3-hydroxyphenyl)-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-(2-chlorophenyl)-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-(2-methoxyphenyl)-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-{2-[2-(dimethylamino)ethoxy]phenyl}-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-{4-[2-(dimethylamino)ethoxy]phenyl}-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-(3-methoxyphenyl)-2-thiophenecarboxamide;

2-[(aminocarbonyl)amino]-5-phenyl-3-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-{4-[2-(1-morpholinyl)ethoxy]phenyl}-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-{4-[2-(1-pyrrolidinyl)ethoxy]phenyl}-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-{4-[2-(1-piperidinyl)ethoxy]phenyl}-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-{4-[3-(dimethylamino)propoxy]phenyl}-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-{3-[2-(dimethylamino)ethoxy]phenyl}-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-{3-[2-(1-morpholinyl)ethoxy]phenyl}-2-thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-{3-[2-(1-pyrrolidinyl)ethoxy]phenyl}-2-

Applicant : Andrew Baxter et al.
Serial No. : 09/868,884
Filed : June 22, 2001
Page : 6 of 14

Attorney's Docket No.: 06275-233001 / Z70663-1P US

3-[(aminocarbonyl)amino]-5-{3-[2-(1-piperidinyloxy)]phenyl}-2-

thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-{3-[3-(dimethylamino)propoxy]phenyl}-2-

thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-{2-[2-(1-morpholino)ethoxy]phenyl}-2-

thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-{2-[2-(1-pyrrolidino)ethoxy]phenyl}-2-

thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-{2-[2-(1-piperidino)ethoxy]phenyl}-2-

thiophenecarboxamide;

3-[(aminocarbonyl)amino]-5-{2-[3-(dimethylamino)propoxy]phenyl}-2-

thiophenecarboxamide;

2-[(aminocarbonyl)amino]-4-methyl-5-(4-chlorophenyl)-3-thiophenecarboxamide;

2-[(aminocarbonyl)amino]-4-methyl-5-(4-methylphenyl)-3-thiophenecarboxamide;

2-[(aminocarbonyl)amino]-4-ethyl-5-phenyl-3-thiophenecarboxamide;

2-[(aminocarbonyl)amino]-4-methyl-5-(4-methoxyphenyl)-3-thiophenecarboxamide;

2-[(aminocarbonyl)amino]-4-methyl-5-(4-fluorophenyl)-3-thiophenecarboxamide;

2-[(aminocarbonyl)amino]-4-methyl-5-(3-fluorophenyl)-3-thiophenecarboxamide;

2-[(aminocarbonyl)amino]-4-methyl-5-(3-methoxyphenyl)-3-thiophenecarboxamide;

2-[(aminocarbonyl)amino]-4-methyl-5-(3-chloro-4-methoxyphenyl)-3-

thiophenecarboxamide;

2-[(aminocarbonyl)amino]-4-methyl-5-(2-chlorophenyl)-3-thiophenecarboxamide;

2-[(aminocarbonyl)amino]-4-methyl-5-(3-trifluoromethylphenyl)-3-thiophenecarboxamide;

Applicant : Andrew Baxter et al.
Serial No. : 09/868,884
Filed : June 22, 2001
Page : 7 of 14

Attorney's Docket No.: 06275-233001 / Z70663-1P US

2-[(aminocarbonyl)amino]-4-methyl-5-(3-methyl-4-methoxyphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(3,5-dimethoxyphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(2,3-dimethoxyphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(4-isopropylphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(3,4,5-trimethoxyphenyl)-3-thiophenecarboxamide;
~~2-[(aminocarbonyl)amino]-4-methyl-5-(2-pyridyl)-3-thiophenecarboxamide;~~
~~2-[(aminocarbonyl)amino]-5-[2-(5-methoxypyridyl)]-4-methyl-3-thiophenecarboxamide;~~
~~2-[(aminocarbonyl)amino]-4-methyl-5-(4-pyrimidyl)-3-thiophenecarboxamide;~~
~~2-[(aminocarbonyl)amino]-4-methyl-5-(2-pyrazinyl)-3-thiophenecarboxamide;~~
2-[(aminocarbonyl)amino]-4-methyl-5-(3,4-dichlorophenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(4-cyanophenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(4-hydroxyphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(4-[2-(1-piperidinyloxy)]phenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-4-methyl-5-(4-[2-(diethylamino)ethoxy]phenyl)-3-thiophenecarboxamide;
~~2-[(aminocarbonyl)amino]-4-methyl-5-(2-furyl)-3-thiophenecarboxamide;~~
2-[(aminocarbonyl)amino]-4-trifluoromethyl-5-phenyl-3-thiophenecarboxamide;
~~2-[(aminocarbonyl)amino]-4-methyl-5-(2-(4-methylthiazolyl))-3-thiophenecarboxamide;~~
2-[(aminocarbonyl)amino]-4-methyl-5-phenyl-3-thiophenecarboxamide;
~~2-[(aminocarbonyl)amino]-4-methyl-5-(3-methyl-isoxazol-5-yl)-3-thiophenecarboxamide;~~
2-[(aminocarbonyl)amino]-5-(4-cyanophenyl)-3-thiophenecarboxamide;

Applicant : Andrew Baxter et al.
Serial No. : 09/868,884
Filed : June 22, 2001
Page : 8 of 14

Attorney's Docket No.: 06275-233001 / Z70663-1P US

2-[(aminocarbonyl)amino]-5-(4-trifluoromethylphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(2,4-difluorophenyl)-3-thiophenecarboxamide;
~~2-[(aminocarbonyl)amino]-5-(2-pyridyl)-3-thiophenecarboxamide;~~
~~2-[(aminocarbonyl)amino]-5-(3-pyridyl)-3-thiophenecarboxamide;~~
~~2-[(aminocarbonyl)amino]-5-[5-(2-methoxypyridyl)]-3-thiophenecarboxamide;~~
2-[(aminocarbonyl)amino]-5-[5-(2,4-dimethoxypyrimidyl)]-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(4-hydroxyphenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(4-chlorophenyl)-3-thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(4-methanesulphonylphenyl)-3-thiophenecarboxamide;
~~2-[(aminocarbonyl)amino]-5-(2-(1-t-butoxycarbonyl)pyrrolyl)-3-thiophenecarboxamide;~~
~~2-[(aminocarbonyl)amino]-5-(2-(5-cyanothienyl))-3-thiophenecarboxamide;~~
~~2-[(aminocarbonyl)amino]-5-(3,5-dimethyl-isoxazol-4-yl)-3-thiophenecarboxamide;~~
~~2-[(aminocarbonyl)amino]-5-(3-furyl)-3-thiophenecarboxamide;~~
~~2-[(aminocarbonyl)amino]-5-(2-pyrrolyl)-3-thiophenecarboxamide;~~
~~2-[(aminocarbonyl)amino]-5-(5-pyrimidinyl)-3-thiophenecarboxamide;~~
~~2-[(aminocarbonyl)amino]-5-(2-(5-chlorothienyl))-3-thiophenecarboxamide;~~
~~2-[(aminocarbonyl)amino]-5-[2-(5-trifluoromethylpyridyl)]-3-thiophenecarboxamide;~~
~~2-[(aminocarbonyl)amino]-5-[2-(5-bromopyridyl)]-3-thiophenecarboxamide;~~
~~2-[(aminocarbonyl)amino]-5-(2-(5-cyanofuryl))-3-thiophenecarboxamide;~~
2-[(aminocarbonyl)amino]-5-(4-[2-(1-piperidinyl)ethoxy]phenyl)-3-
thiophenecarboxamide;
2-[(aminocarbonyl)amino]-5-(4-[2-(1-(2,2,6,6-tetramethyl)piperidinyl)ethoxy]phenyl)-3-
thiophenecarboxamide;

Applicant : Andrew Baxter et al.
Serial No. : 09/868,884
Filed : June 22, 2001
Page : 9 of 14

Attorney's Docket No.: 06275-233001 / Z70663-1P US

2-[(aminocarbonyl)amino]-5-(4-(thiazol-4-yl-methoxy)phenyl)-3-thiophenecarboxamide;

2-[(aminocarbonyl)amino]-5-(4-[2-(dimethylamino)ethoxy]phenyl)-3-thiophenecarboxamide;

2-[(aminocarbonyl)amino]-5-(4-[2-(diethylamino)ethoxy]phenyl)-3-thiophenecarboxamide;

2-[(aminocarbonyl)amino]-5-(4-[2-(1-morpholinyl)ethoxy]phenyl)-3-thiophenecarboxamide;

~~2-[(aminocarbonyl)amino]-5-(2-furyl)-3-thiophenecarboxamide;~~

~~2-[(aminocarbonyl)amino]-5-(2-(5-methylfuryl))-3-thiophenecarboxamide;~~

~~5-[(aminocarbonyl)amino]-2-(3,5-dichlorophenyl)-1,3-oxazole-4-carboxamide;~~

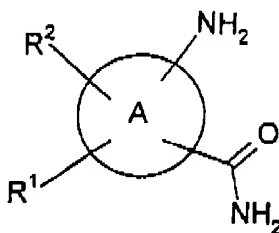
~~5-[(aminocarbonyl)amino]-2-(4-trifluoromethylphenyl)-1,3-oxazole-4-carboxamide;~~

2-[(aminothiocarbonyl)amino]-5-phenyl-3-thiophenecarboxamide;

and pharmaceutically acceptable salts and solvates thereof.

9. (Previously presented) A process for the preparation of a compound of formula (I), according to claim 1, which comprises:

(a) reaction of a compound of formula (II):



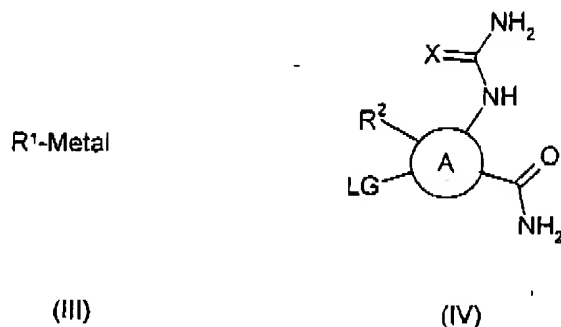
(II)

wherein A, R¹ and R² are as defined in Claim 1 with an isocyanate (X = O) or an isothiocyanate (X = S); or

Applicant : Andrew Baxter et al.
Serial No. : 09/868,884
Filed : June 22, 2001
Page : 10 of 14

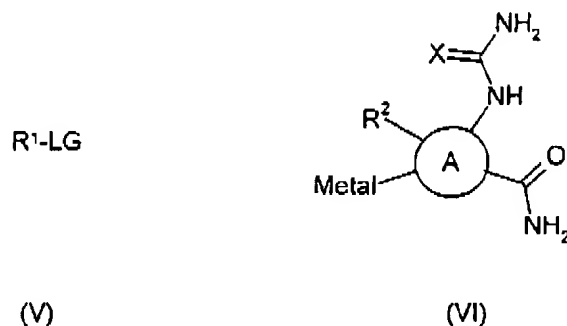
Attorney's Docket No.: 06275-233001 / Z70663-1P US

(b) reaction of compound of formula (III) with a compound of formula (IV)



wherein A, X, R¹ and R² are as defined in Claim 1 and LG represents a leaving group; or

(c) reaction of compound of formula (V) with a compound of formula (VI)



wherein A, X, R¹ and R² are as defined in Claim 1 and LG represents a leaving group;

and where necessary converting the resultant compound of formula (I), or another salt thereof, into a pharmaceutically acceptable salt thereof; and where desired converting the resultant compound of formula (I) into an optical isomer thereof.

Applicant : Andrew Baxter et al.
Serial No. : 09/868,884
Filed : June 22, 2001
Page : 11 of 14

Attorney's Docket No.: 06275-233001 / Z70663-1P US

10. (Previously presented) A pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in claim 1, in association with a pharmaceutically acceptable adjuvant, diluent or carrier.

11. (Previously presented) A process for the preparation of a pharmaceutical composition which comprises mixing a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in claim 1 with a pharmaceutically acceptable adjuvant, diluent or carrier.

12.-19. Canceled

20. (Previously presented) A method of treating an IKK2 mediated disease which comprises administering to a patient a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in claim 1.

21. (Previously presented) A method of treating an inflammatory disease in a patient suffering from, or at risk of, said disease, which comprises administering to the patient a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in claim 1.

22. (Original) A method according to claim 21, wherein the disease is asthma.

23. (Original) A method according to claim 21, wherein the disease is rheumatoid arthritis.

24. (Original) A method according to claim 21, wherein the disease is multiple sclerosis.

Applicant : Andrew Baxter et al.
Serial No. : 09/868,884
Filed : June 22, 2001
Page : 12 of 14

Attorney's Docket No.: 06275-233001 / Z70663-1P US

25. (Original) A method according to claim 21, wherein the disease is chronic obstructive pulmonary disease.

26. (Previously presented) A pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in claim 8, in association with a pharmaceutically acceptable adjuvant, diluent or carrier.